rats, atrial stretch induces a rapid increase in BNP mRNA but not in ANP mRNA, although both peptides are released.[4] The secretion of BNP seems to result from increased gene expression. This might explain the clinical observation that intravenous saline loading raises plasma ANP but not plasma BNP within 60 minutes, but ingestion of salt tablets raises the plasma concentration of both peptides after 5 days.[5] Indeed, the response of plasma BNP to saline loading is slower than the ANP response in patients with right ventricular failure (Morice AH, personal communication). Further studies of the relation between BNP and volume status may shed light on this important subject.

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1 Yoshimura M, Yasue H, Tanaka H, Kikuta K, Sumida H, Kato H, *et al.* Responses of plasma concentrations of A type natriuretic peptide and B type natriuretic peptide to alacepril, an angiotensin-converting enzyme inhibitor, in patients with congestive heart failure. *Br Heart J* 1994;72:528–33.
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This letter was shown to the author, who replies as follows:

SIR,—Plasma concentrations of ANP and BNP increase in patients with heart failure and correlate well with the degree of left ventricular function in patients with chronic heart failure.[1] Plasma concentrations of ANP and BNP both increase as the heart becomes overloaded. However, ANP concentrations increase before BNP concentrations.[2,3] Plasma ANP increases mainly through secretion from vesicles that store ANP in the atria (regulated pathway). None the less, BNP mRNA is expressed earlier than ANP mRNA.[3] This is probably because BNP mRNA has the characteristics of an acute phase reactant whereas ANP mRNA does not.[4,5] Clinical studies showed that BNP is secreted mainly from the ventricles in normal subjects and patients with heart failure.[1] Though we can not disregard the amount of BNP secreted by the atria, nearly all the circulating BNP originates from the ventricles.

I and my colleagues showed that the time courses of changes in plasma ANP and plasma BNP were different when cardiac overload was reduced by administration of an angiotensin-converting enzyme inhibitor.[6] The mechanism is probably related to the different secretion sites and pathways of ANP and BNP: ANP is mainly secreted by a regulated pathway in the atria and BNP by a constitutive pathway in the ventricles. Other factors may also be involved in the mechanisms—for example, the direct action of angiotensin-converting enzyme inhibitor on the degradation of ANP and BNP. Thus the mechanisms of the changes in plasma ANP and BNP may vary when the cardiac load is increasing and decreasing. As Dr Cheung indicates, regulation of the natriuretic peptide system is important and complex. The mechanisms responsible for the changes in plasma ANP and BNP involve different patterns of synthesis, storage, secretion, and degradation.

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1 Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M, Ogawa H, Okumura K, Mukoyama M, Nakao K. Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. *Circulation* 1994;90:195–203.
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Transcatheter occlusion of cardiac defects

SIR,—Gatzoulis, Redington, and Rigby *et al* reported their experience with transcatheter occlusion of the ductus arteriosus[1] and of atrial[2] and ventricular[3] septal defects with the Rashkind ductal umbrella device. We are somewhat surprised that they made no mention of the buttoned device that we and others used in transcatheter occlusion of the ductus arteriosus[4] and atrial septal defect.[5–7] We now have considerable experience with this device in nearly 400 patients with atrial septal defects, 120 patients with a patent ductus arteriosus (PDA), and eight patients with ventricular septal defects (unpublished observations).

Patent ductus arteriosus—Our experience with the buttoned device[4,8] indicates that it has several advantages over the Rashkind device. Gatzoulis *et al* had to exclude large tubular ducts with no obvious stenosis at the pulmonary end.[1] All sizes and types of ductus[4,8] can be successfully closed with the buttoned device because it is adjustable. In all infants and children we were able to implant the device through a 7F delivery sheath rather than 8F and 11F sheaths, which had to be used in most of Gatzoulis's patients. The success rate for device implantation was 86% for the Rashkind device and 97·5% for the buttoned device. Problems such as embolisation into the left pulmonary artery, inability to occlude the duct satisfactorily, and severe haemolytic anaemia reported by Gatzoulis were not seen in our 120 patients. Residual shunts on colour flow mapping, particularly in infants who had 17 mm Rashkind umbrella devices implanted were higher than those that we saw with the buttoned device. Finally, there has been increasing concern about the development of stenosis of the left pulmonary artery after implantation of the Rashkind device, especially in young children. Thus the buttoned device seems to have several advantages over the Rashkind device and it is hoped that, with further clinical trials, the buttoned device will prove to be useful in transcatheter occlusion of arterial ducts of all types and sizes.

Atrial septal defect—Redington and Rigby[2] modified the Rashkind PDA occluder and used it to close interatrial communications of various types. Of the 11 patients with fenestrated Fontan, there were two (18%) procedural failures. They were successful in closing the defect in two of the four patients with left-to-right shunts; the two remaining patients required surgical removal of the device and closure of the defect. In our more recently reported experience, which analysed the data of the first 180 patients,[9] 14 devices (7·7%) were dislodged. The dislodgement rate has improved with experience and with successive generations of the device. First and second generation devices became dislodged in about 10% of patients. However, in the third generation device the device dislodgement rate was 3·1% (2 of 65)[9]; this has further decreased to less than 1% in the fourth generation buttoned device (unpublished observations). Redington and Rigby placed a bend in the arm of the device. Such a bend is thought to be the reason why the arms of the clamshell device broke and why the device was withdrawn from clinical trials.

Ventricular septal defect—Rigby and Redington concluded that their data do not support the routine use of a Rashkind PDA occluder to close perimembranous ventricular septal defects. We agree. Our own experience in occluding ventricular septal defect with buttoned device, though successful, is limited. Therefore, we cannot draw definitive conclusions on the superiority of the buttoned device.

In conclusion, the reports of Gatzoulis, Redington and Rigby[1–3] showed the usefulness of the Rashkind PDA occluder in highly selected patient subgroups. We submit that the buttoned device has a greater utility in a wider range of patient subsets, although definite conclusions can only be drawn after longer clinical trials.

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1 Gatzoulis MA, Rigby ML, Redington AN. Umbrella occlusion of persistent arterial duct in children under two years. *Br Heart J* 1994;72:364–7.

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This letter was shown to the authors, who reply as follows:

SIR,—We thank Dr Rao and Dr Sideris for updating us on the results of the most recent modification of their buttoned devices. We appreciate that things may have changed over the past year or so: when we submitted our papers[1-3] there was little up to date information on the buttoned device and we did not feel compelled to cite limited peer review data, abstracts, or unpublished observations. None the less, these earlier data, representing their learning curve, are perhaps more directly relevant to our data.

Patent arterial duct—The initial report of the adjustable buttoned device[4] concerned 14 patients and was published only one month before we submitted our study. We accept we should have referenced this paper, although only one of the patients was less than 2 years old (a criterion for entering our study) and all of the devices were implanted via a 7F guiding catheter. Two of their patients had a residual shunt on follow up colour Doppler (14%), a rate similar to our own residual patency rate. Furthermore we made the point that the modified Rashkind device can be delivered through a 6F catheter, which may be useful in these very small children. We, like Rao and Sideris, look forward to further clinical trials with the buttoned device, but for the time being we believe that the more familiar Rashkind umbrella has proved to be a more reasonable alternative in this select group of patients.

Interatrial communications—Some peer reviewed data were not available to us when we submitted our paper in October 1993. The multi-Institutional US trial,[5] reports the intention to treat data in 57 patients. In seven patients the procedure was abandoned, urgent surgical retrieval was necessary in four because the position of the device was unstable, and there was late unbuttoning in another. Thus the overall failure rate was approximately 20%. The experience with a later modification of the device seems to be better and we note the unpublished observation of a 1% failure rate with the fourth generation device. However, most of the interatrial communications reported in our paper were in patients who underwent fenestrated total cavopulmonary connections, whereas Rao and Sideris report their experience with only naturally occurring atrial shunts. We are not sure whether the design of the buttoned device is ideal for closure of fenestrations, particularly when an intra-atrial tube or baffle has been used. The modified Rashkind device seems to be ideal under these circumstances, and concern about stress fractures of the arms is less pressing in view of the static nature of the material.

Ventricular septal defects—We are informed that eight patients have undergone "successful" occlusion of a ventricular septal defect with the buttoned device. Quite clearly we could not have been expected to cite these unpublished data. We await a full report of their intention to treat and follow up data in this group of patients.

The technique of delivery of the Rashkind PDA occluder is well known to most units undertaking interventional catheterisation. Our papers describe modifications that broaden the indications for the use of a device, which is readily available to many. It is clearly not a panacea, and is not proposed as such. The original indications for the buttoned device appear to be widening, and it may prove to be an acceptable all-purpose device. Nonetheless, all interventional cardiologists need to be aware of the implications (both medical and non-medical) of the approaches that they adopt. Product liability remains a concern for both the modified Rashkind and the buttoned device, and may ultimately prove to be a decisive factor in the development of all interventional devices.[6] Never before has careful and accurate reporting of results been more necessary. In this respect we have no reservations regarding our three papers.

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1 Gatzoulis MA, Rigby ML, Redington AN. Umbrella occlusion of persistent arterial duct in children under two years. *Br Heart J* 1994;72:364–7.
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Nitrates and severe aortic stenosis

SIR,—There is concern about using nitrates in patients with severe aortic stenosis. Standard textbooks on cardiovascular medicine[1] and prescribing recommendations[2] suggest that nitrates and other vasodilators are contraindicated in patients with severe aortic stenosis, though there is little published evidence for this. We describe a patient with severe aortic stenosis, left ventricular impairment, and severe cardiac failure in whom nitrate administration improved cardiac filling pressures without worsening the transaortic valve gradient.

A 74 year old man was admitted with a 3 month history of progressive dysnoea, orthopnoea, and paroxysmal nocturnal dyspnoea. Electrocardiography (ECG) showed left ventricular hypertrophy and strain and echocardiography showed severe calcific aortic stenosis and a dilated left ventricle with impaired systolic function. A chest *x* ray showed considerable cardiomegaly with pulmonary oedema. He was treated acutely with intravenous diuretics and digoxin.

After stabilisation of his heart failure, left heart catherisation was performed on day 9. This showed normal coronary arteries, but global left ventricular impairment with a left ventricular end diastolic filling pressure (LVEDP) of 36 mm Hg. The left ventricular systolic pressure was 205 mm Hg, while the aortic pressure was 100/55 mm Hg. The transaortic valve gradient was 105 mm Hg, consistent with severe aortic stenosis. No aortic regurgitation was present. The patient started to feel breathless (while lying flat) during the procedure and sublingual nitrates were given (glyceryl trinitrate spray, 2 doses or 800 μg). The LVEDP fell to 20 mm Hg and the patient's symptoms improved considerably. After nitrate administration there was no significant change in the gradient across the aortic valve and only a 5 mm Hg fall in aortic systolic pressure.

This case suggests that nitrate administration needs to be explored as a treatment in patients with severe aortic stenosis and cardiac failure. Nitrate use may reduce cardiac preload and concomitantly improve cardiac output and the myocardial oxygen supply/demand ratio. Nitrates should have additional advantages if coronary artery disease is present. We believe that further studies are needed of treatment with nitrates in patients with aortic stenosis.

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NOTICE

The 1996 Annual Meeting of the **British Cardiac Society** will take place at the Scottish Exhibition & Conference Centre, Glasgow from 7 to 9 May.